

Applicant : Yaakov Naparstek  
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Filed : April 4, 2001  
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**Remarks**

Claims 8-10 were pending in the subject application. By this Amendment, applicant has added new claims 11-14. Accordingly, claims 8-14 are pending in the subject application.

Support for new claims 11-13 may be found, *inter alia*, on page 18, lines 3 to page 19, line 10 of the subject application.

Support for new claim 14 may be found, *inter alia*, on page 4, lines 29-32, on page 11, line 21 to page 12, line 14, and in Figures 5, 6, 7 and 9 of the subject application.

New claim 14 is supported by portions of the disclosure having a March 20, 1997 priority date and, as such, are not subject to the rejection of record relying on art after March 20, 1997.

**Rejections under 35 U.S.C. §103(a)**

In the January 30, 2006 Office Action, the Examiner maintained the rejection of claims 8-10 under 35 U.S.C. §103(a) as allegedly unpatentable over Gaubitz, M., et al., Journal of Autoimmunity, (1999), 11:495-501 ("Gaubitz") in view of U.S. Patent No. 6,228,363, issued May 8, 2001 (Naparstek) with a priority date of March 20, 1998 ("the '363 patent") and Madaio, M., et al., Journal of the American Society of Nephrology, (1996), 7:387-396 ("Madaio").

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The Examiner stated that applicant's November 15, 2005 response has been fully considered but is not persuasive. The Examiner selectively comments on applicants' November 15, 2006 remarks, but does not address all of applicants' reasons for patentability. The rejection of record continues to lack an explanation of how the combined disclosure of the cited references teaches every element of a rejected claim.

Specifically, the combined references fail to teach the element of "extracorporeal treatment of plasma ... by affinity absorption column chromatography, wherein the column comprises a peptide having an amino acid sequence as set forth in SEQ. ID. NO. 1." A more detailed analysis follows:

1. Extracorporeal Removal Of Antibodies That Bind To A Peptide Represented By SEQ ID NO. 1 Is Neither Taught Nor Suggested By The Cited References As A Treatment For Lupus.

The combined disclosure of the references offers no suggestion to prepare a column with the peptide of SEQ ID NO. 1 (R38 peptide) for the purpose of extracorporeal treatment of plasma. SEQ ID NO. 1 is only disclosed in the cited references for administration to a patient.

The January 30, 2006 Office Action does not contradict that the cited art, when combined, fails to teach this element. Indeed, it does not even address this deficiency of the rejection of record. However, the Examiner is certainly aware that a proper obviousness rejection must show that each and every element of a rejected claim appears in the

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art as combined. Because the January 30, 2006 Office Action does not explain the presence of at least one element of the rejected claim in the combined art, the rejection is improper.

For completeness of these remarks, Applicant notes that in a December 20, 2004 Office Action (but no longer in the January 30, 2006 Office Action), the Examiner relied on Gaubitz et al. and Madaio et al. for the elements of "extracorporeal removal" and "laminin". These two references do not mention the R38 peptide (SEQ ID NO 1). A third reference, the '363 patent, discloses the R38 peptide, but does so only for administration. Thus, previous statements of the rejection also failed to clearly specify how a combination of the cited references teaches the element of extracorporeal removal of anti-R38 antibodies.

Applicant also notes that in the December 20, 2004 Office Action (but no longer in the January 30, 2006 Office Action), the Examiner's attempted to equate "laminin" with the R38 peptide. They are not the same. For one, laminin is significantly larger. Therefore, whatever Gaubitz et al. and Madaio et al. taught with respect to laminin cannot be applied to the smaller R38 peptide.

Applicant further notes that in the December 20, 2004 Office Action (but no longer in the January 30, 2006 Office Action), the Examiner alleged that "one of ordinary skill in the art ... would have been motivated to employ the R38 peptide on an immunoadsorption column given the teachings of Madaio et al." Here, the Examiner is advancing the

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disallowed "obvious to try" theory. It is well settled, however, that references which might make something obvious to try, do not make an invention unpatentable under 35 U.S.C. § 103 without a clear motivation and expectation of success. The combined cited references do not motivate, and certainly do not offer an expectation of success of, an extracorporeal treatment using the R38 peptide.

Accordingly, applicants maintain their position that, in the absence of applicant's disclosure of extracorporeal removal using the R38 peptide, one of skill in the art would understand R38 to be useful for administration to lupus patients as disclosed in the '363 patent. It is only in hindsight with the benefit of applicant's disclosure that the Examiner has come to believe the R38 peptide may be used in a column for extracorporeal removal of anti-R38 antibodies. The combination of cited references clearly lacks this element of the claimed invention.

Accordingly, the rejection based on Gaubitz et al., the '363 patent, and Madaio et al. is improper and should be withdrawn.

2. Binding of an Antibody on a Plate in an ELISA Test Offers No Expectation of Binding in a Column.

Applicant has previously explained that the binding of an antibody to the R38 peptide on a plate in an ELISA test does not mean the same antibody will bind an R38 peptide attached to a Sepharose® bead.

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The January 30, 2006 Office Action dismissed applicant's explanation on the sole basis that "antibody ligands have been routinely attached to Sepharose beads for 30+ years." Applicant respectfully points out that this misses the point of applicant's prior explanation. At minimum, 1) differences in the conformational structure of the peptide on the plate versus the peptide on the bead, and 2) different time period of contact between the peptides on an ELISA plate versus that on a column, should be taken into account.

Applicants maintain their position that whatever was done for 30+ years does not provide the expectation of success in the context of applicant's R38 peptide necessary for a proper rejection under 35 U.S.C. § 103, for the reasons applicants previously explained.

### 3. The subject invention can be scaled up.

On page 4 of the January 30, 2006 Office Action, the Examiner dismissed the inventor's rule 132 Declaration on the basis that the Declaration shows data after the filing date, and purportedly does not show anything unpredictable. Applicant admits to some confusion.

Applicant submitted the Declaration to show that applicant's Example 12 in the specification can be successfully scaled up, as the heading of the section discussing the Declaration indicated. The question of scale-up was first presented by the Examiner on page 4 of the December 20, 2006 Office Action, where the Examiner argued that applicant's 30-60% removal of pathogenic anti-

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R38 antibodies from plasma in Example 12 of the specification cannot be predictive of a scaled-up treatment method. The Declaration was submitted to address this question.

Now, the Examiner dismisses the Declaration for presenting results obtained after the filing date. Certainly the Examiner is aware that a patent application is a constructive reduction to practice as of its filing date. To the extent there was any doubt that Example 12 of the application as filed is predictive of a treatment method, the Declaration removes such doubt. In so doing, the Declaration confirms that the 30-60% removal rate of pathogenic anti-R38 antibodies shown in Example 12 can be repeated upon scale-up.

As for unexpected results, Example 12 of the application provides the unexpected results with the R38 peptide, the Declaration merely confirms the results upon scale-up, as predicted by the application as filed.

Applicant notes the Examiner's reference to Gaubitz et al. purporting to show removal of up to 70% of antibodies from a patient. However, as explained previously, the results of Gaubitz et al. cannot be compared to applicant's results. Gaubitz et al. did not target the anti-R38 antibody. Applicant, on the other hand targeted the anti-R38 antibody and removed 30-60% of such anti-R38 antibodies. One certainly could not have predicted this from art which does not even mention extracorporeal removal of anti-R38 antibodies.

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Finally, the Examiner also alleged that applicant's apparent arguing of unexpected results indicates an admission that the invention is obvious. Applicant respectfully submits that such a gratuitous assumption does not help advance this application, and does not narrow issues for appeal. Clearly, no admission was made by applicant. Applicant has submitted the Declaration for the reasons explained above, and to have a full and complete record.

Accordingly applicant maintains that claim 8-10 are not obvious over Gaubitz in view of the '363 patent and Madaio, and requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. 103(a).

Applicant further submits that new claims 11-13 are not obvious over Gaubitz in view of the '363 patent and Madaio, and that new claim 14 is not subject to the cited art because it is supported by the March 20, 1997 priority disclosure.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

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No fee other than the enclosed \$1,020.00 fee for the three-month extension of time is deemed necessary in connection with the filing of this Amendment and a check in that amount is enclosed. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

*Gary J. Gershik* 7/27/06  
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